

compared to the Master Reference, of not greater than 1.0 as established by: independent parallel line assays with five or more replicates; or other valid assay methods for determining relative antigen content which demonstrate linearity, specificity, and reproducibility at least equivalent to the parallel line assay and are acceptable to the Animal and Plant Health Inspection Service.

(2) Qualifying serials used to requalify or extend the dating period of a Master Reference shall be determined to be immunogenic in accordance with methods deemed appropriate by the Animal and Plant Health Inspection Service as provided in paragraph (a)(1) of this section, and, in addition, shall be within their permitted dating period and have been prepared in accordance with the production method described in the currently filed Outline of Production.

(r) *Immunogenicity*. The ability of a biological product to elicit an immune response in animals as determined by test methods or procedures acceptable to the Animal and Plant Health Inspection Service.

[38 FR 8426, Apr. 2, 1973, as amended at 40 FR 45419, Oct. 2, 1975; 41 FR 6751, Feb. 13, 1976; 43 FR 3701, Jan. 27, 1978; 56 FR 66782, 66783 Dec. 26, 1991; 62 FR 19037, Apr. 18, 1997]

#### § 101.6 Cell cultures.

When used in conjunction with or in reference to cell cultures, which may be referred to as tissue cultures, the following terms shall mean:

(a) *Batches of primary cells*. A pool of original cells derived from normal tissue up to and including the 10th subculture.

(b) *Cell line*. A pool of cells which are 11 or more subcultures from the tissue of origin.

(c) *Subculture*. Each flask to flask transfer or passage regardless of the number of cell replications.

(d) *Master Cell Stock (MCS)*. The supply of cells of a specific passage level from which cells for production of biologics originate.

[38 FR 8426, Apr. 2, 1973, as amended at 40 FR 45419, Oct. 2, 1975; 49 FR 22624, May 31, 1984]

#### § 101.7 Seed organisms.

When used in conjunction with or in reference to seed organisms, the following shall mean:

(a) *Master Seed*. An organism at a specific passage level which has been selected and permanently stored by the producer from which all other seed passages are derived within permitted levels.

(b) *Working Seed*. An organism at a passage level between Master Seed and Production Seed.

(c) *Production Seed*. An organism at a specified passage level which is used without further propagation for initiating preparation of a fraction.

[49 FR 22625, May 31, 1984]

### PART 102—LICENSES FOR BIOLOGICAL PRODUCTS

#### Sec.

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AUTHORITY: 21 U.S.C. 151–159; 7 CFR 2.22, 2.80, and 371.2(d).

#### § 102.1 Licenses issued by the Administrator.

Each establishment qualified to prepare biological products under the Virus-Serum-Toxin Act shall hold an unexpired and unrevoked U.S. Veterinary Biologics Establishment License issued by the Administrator and a U.S. Veterinary Biological Product License for each product prepared in such establishment unless the product is subject to the provisions of 9 CFR parts 103 or 106 of this subchapter.

[60 FR 48021, Sept. 18, 1995]

#### § 102.2 Licenses required.

(a) Every person who prepares biological products subject to the Virus-Serum-Toxin Act shall hold an unexpired, unsuspended, and unrevoked U.S. Veterinary Biologics Establishment License and at least one unexpired, unsuspended, and unrevoked U.S. Veterinary Biological Product License issued

by the Administrator to prepare a biological product.

(b) An applicant who applies for an establishment license must also apply for at least one product license. An establishment license will not be issued without a license authorizing the production of a biological product in the establishment.

[52 FR 11026, Apr. 7, 1987, as amended at 56 FR 66783, Dec. 26, 1991; 61 FR 52873, Oct. 9, 1996]

### § 102.3 License applications.

(a) *U.S. Veterinary Biologics Establishment License.* (1) The operator of each establishment of the kind specified in § 102.2 shall make written application to the Administrator for a license. Blank forms of application will be furnished upon request to Animal and Plant Health Inspection Service.

(2) When a person conducts more than one establishment, a separate application shall be made for each establishment.

(3) Whenever subsidiaries are to operate in an establishment for which license application is made, the applicant shall apply for permission for such subsidiaries to operate in the establishment and furnish therewith a complete statement regarding the relationship between the applicant and the subsidiaries.

(4) Facilities documents, prepared as prescribed in part 108 of this subchapter, shall accompany the application for license unless previously filed with Animal and Plant Health Inspection Service.

(5) Each application for a U.S. Veterinary Biologics Establishment License shall be accompanied by an application for one or more U.S. Veterinary Biological Product Licenses and the supporting documents required by paragraph (b)(2) of this section.

(6) A new application shall be made when a change of ownership, operation, or location of an establishment occurs; or prior to the expiration of a U.S. Veterinary Biologics Establishment License issued for an interim period of time.

(b) *U.S. Veterinary Biological Product License.* (1) The licensee of each establishment or applicant for an establishment license shall make written appli-

cation to the Administrator for a U.S. Veterinary Biological Product License for each biological product to be prepared in the licensed establishment.

(2) Each application for a U.S. Veterinary Biological Product License shall be supported by:

(i) At least four copies of an Outline of Production prepared in accordance with §§ 114.8 and 114.9 of this subchapter; and

(ii) At least three copies of test reports and research data sufficient to establish purity, safety, potency, and efficacy of the product; and

(iii) Legends prepared as prescribed in § 108.5 of this subchapter designating which facilities are to be used in the preparation of each fraction; and

(iv) Labels in finished form or sketches prepared as prescribed in § 112.5 of this subchapter, together with information regarding all claims to be made on labels and in advertising matter to be used in connection with or related to the biological product.

(Approved by the Office of Management and Budget under control number 0579-0013)

[39 FR 37763, Oct. 24, 1974, as amended at 48 FR 57472, Dec. 30, 1983; 49 FR 21043, May 18, 1984; 50 FR 50763, Dec. 12, 1985; 56 FR 66783, Dec. 26, 1991]

### § 102.4 U.S. Veterinary Biologics Establishment License.

(a) Before a U.S. Veterinary Biologics Establishment License will be issued by the Administrator for any establishment, an inspection shall be made to determine whether the condition, equipment, facilities, and the like, of the establishment, and the methods used to prepare biological products are in conformity with the requirements in the regulations.

(b) A license shall not be issued unless:

(1) In the opinion of the Administrator, the condition of the establishment, including its facilities, and the methods of preparation of biological products are such as reasonably to assure that the products shall accomplish the purpose for which they are intended; and

(2) The Administrator is satisfied on the basis of information before him that: